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Date Mailed: June 11, 2003 U.S. Appl. Ser. No.: 09/975,308

Inventors: Friddle et al

Title: Novel Human TTM Proteins and Polynucleotides Encoding the Same

Attorney Docket No.: LEX-0252-USA

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Application Number	09/975,308
Filing Date	Oct 11, 2001
First Named Inventor	Friddle, Carl Johan
Group Art Unit	1646
Examiner Name	R. Li
Attorney Docket Number	LEX-0252-USA

ENCLOSURES *(check all that apply)*

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PETITION FOR EXTENSION OF TIME UNDER 37 CFR 1.136(a)

Docket Number (Optional) LEX-0252-USA

In re Application of	Friddle et al.
Application Number 09/975,308	Filed 10/11/2001
For	Novel Human 7TM Proteins and Polynucleotides Encoding the Same
Group Art Unit 1646	Examiner R. Li

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a reply in the above identified application.

The requested extension and appropriate non-small-entity fee are as follows (check time period desired):

☒ One month (37 CFR 1.17(a)(1)) $ 55.00

☒ Applicant claims small entity status. See 37 CFR 1.27.

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☐ assignee of record of the entire interest. See 37 CFR 3.71.
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☒ attorney or agent under 37 CFR 1.34(a).
Registration number if acting under 37 CFR 1.34(a). 41,866.

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REG. NO. 41,071

Lance K. Ishimoto Reg. No. 41,866
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June 11, 2003
Date

Signature (Lance K. Ishimoto by David W. Hiller)
DAVID W. HIBLER
REG. NO. 41,071

Lance K. Ishimoto Reg. No. 41,866
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Friddle *et al.*		
Serial No.:	09/975,308	Group Art Unit:	1646
Filed:	10/11/2001	Examiner:	R. Li
For:	Novel Human 7TM Proteins and Polynucleotides Encoding the Same	Attorney Docket No.:	LEX-0252-USA

APPEAL BRIEF

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Assistant Commissioner for Patents
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APPEAL BRIEF

Sir:

Appellants hereby submit an original and two copies of this Appeal Brief to the Board of Patent Appeals and Interferences ("the Board") in response to the Final Office Action mailed on November 4, 2002. The Notice of Appeal was timely submitted on March 4, 2003, and was received in the Patent and Trademark Office ("the Office") on March 11, 2003. This Appeal Brief is timely submitted in light of the concurrently filed Petition for an Extension of Time of one month to and including June 11, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(1) from Appellants' Representatives' deposit account. The Commissioner is also authorized to charge the fee for filing this Appeal Brief ($160.00), as required under 37 C.F.R. § 1.17(c), to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

Appellants believe no fees in addition to the fee for filing the Appeal Brief and the fee for the extension of time are due in connection with this Appeal Brief. However, should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason related to this communication, the Commissioner is authorized to charge any underpayment or credit any overpayment to Lexicon Genetics Incorporated Deposit Account No. 50-0892.

I. REAL PARTY IN INTEREST

The real party in interest is the Assignee, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, Texas, 77381.

II. RELATED APPEALS AND INTERFERENCES

Appellants know of no related appeals or interferences that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

The present application was filed on October 11, 2001, claiming the benefit of U.S. Provisional Application Number 60/239,592, which was filed on October 11, 2000, and included original claims 1 and 2. A Restriction and Election Requirement was issued on May 7, 2002, separating the original claims into sixteen separate and distinct inventions. In a response to the Restriction and Election Requirement submitted to the Office on June 3, 2002, Appellants elected with traverse the claim of the Group IV invention (original claim 1 (in part)) for prosecution on the merits, argued that the Group XII invention (original claim 2 (in part)) should be properly rejoined with the Group IV invention, and amended claims 1 and 2 to remove reference to the Group I-III, V-XI and XII-XVI inventions.

A First Official Action on the merits ("the First Action") was issued on July 8, 2002, in which the Examiner agreed that the Group XII invention should be rejoined with the Group IV invention, claims 1 and 2 were rejected under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and claims 1 and 2 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. In a response to the First Official Action submitted to the Office on October 7, 2002 ("Response to the First Action"), Appellants addressed the rejections of claims 1 and 2, and added new claim 3.

A Second and Final Official Action ("the Final Action") was mailed on November 4, 2002, maintaining the rejection of claims 1-3 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. In a response to the Second and Final Office Action submitted on March 4, 2003 ("Response to the Final Action"), Appellants again addressed the rejections of claims 1-3. An Advisory Action ("the Advisory Action") was mailed on April 15, 2003, maintaining the rejection of claims 1-3 under 35 U.S.C. § 101 as allegedly lacking a patentable utility, and under 35 U.S.C. § 112, first paragraph as allegedly unusable by the skilled artisan due to the alleged lack of patentable utility. Therefore, claims 1-3 are the subject of this appeal. A copy of the appealed claims are included below in the Appendix (Section IX).

IV. STATUS OF THE AMENDMENTS

As no amendments subsequent to the Final Action have been filed, Appellants believe that no outstanding amendments exist.

V. SUMMARY OF THE INVENTION

The present invention relates to Appellants' discovery and identification of novel human polynucleotide sequences that encode novel seven transmembrane protein receptor proteins, specifically G-protein coupled receptors (GPCRs) (specification at page 2, lines 8-11). GPCRs have been associated with transduction pathways involving G-proteins or PPG proteins (specification at page 2, lines 2-3).

The presently claimed polynucleotide sequences were compiled from human genomic sequences in conjunction with cDNAs generated from human skeletal muscle, testis, and spleen mRNAs (specification at page 5, lines 28-30).

The specification details a number of uses for the presently claimed polynucleotide sequences, including in diagnostic assays such as forensic analysis (see, for example, the specification at page 4, line 31, page 36, lines 30-31, and page 38, lines 4-5), in assessing gene expression patterns, particularly using a high throughput "chip" format (see, for example, the specification at page 10, lines 13-16), and in mapping the sequences to a specific region of a human chromosome (see, for example, the specification at page 4, lines 24-26).

VI. ISSUES ON APPEAL

1. Do claims 1-3 lack a patentable utility?
2. Are claims 1-3 unusable by a skilled artisan due to a lack of patentable utility?

VII. GROUPING OF THE CLAIMS

For the purposes of the outstanding rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, the claims will stand or fall together.

VIII. ARGUMENT

A. Do Claims 1-3 Lack a Patentable Utility?

The Final Action first rejects claims 1-3 under 35 U.S.C. § 101, as allegedly lacking a patentable utility due to not being supported by either a specific and substantial or a well-established utility.

Appellants pointed out in both the Response to the First Action and the Response to the Final Action that as just one example of the utility of the presently claimed sequences, the present nucleic acid sequences have utility in forensic analysis, as described in the specification as originally filed (see, for example, page 4, line 31, page 36, lines 30-31, and page 38, lines 4-5). As described in the specification at page 8, lines 25-28, the present sequences define a coding single nucleotide polymorphism - specifically, a G/A polymorphism at position 146 of SEQ ID NO:8, which can lead to a serine or asparagine residue at amino acid position 49 of SEQ ID NO:9. As such polymorphisms are the basis for forensic analysis, which in undoubtedly a "real world" utility, the presently claimed sequences must in themselves be useful.

The Advisory Action states that the use of the presently described polymorphism in forensic analysis would require "further research", because "the instant disclosure fails to disclose the population that polymorphic marker distinguishes" (the Advisory Action at page 2). Appellants submit that the presently described polymorphism is useful in forensic analysis **exactly as it was described in the specification as originally filed**. Individual members of a population can be distinguished based on the presence or absence of the described polymorphism, and thus, these sequences are useful without "additional research". Simply because the use of this polymorphic marker will necessarily provide additional information on the percentage of particular subpopulations that contain this polymorphic marker does not mean that "additional research" is needed in order for this marker as it is presently described in the instant specification to be of use to forensic science. Thus, the Examiner's position does not support the alleged lack of utility.

This is also not a case of a potential utility. As stated above, using the presently described polymorphic marker as described in the specification as originally field will definitely distinguish members of a population from one another. In the worst case scenario, this marker is useful to distinguish 50% of the population (in other words, the marker being present in half of the population). The ability to eliminate

50% of the population from a forensic analysis **clearly** is a real world, practical utility. In the Advisory Action, the Examiner states that the use of the presently described polymorphic marker in forensic analysis is not "specific and substantial" (the Advisory Action at page 2). Appellants are completely at a loss to understand how, given the widespread and daily use of forensic analysis to distinguish individuals, the use of a polymorphic marker in forensic analysis is not a "substantial" use. With regard to the allegation that the use of the presently described polymorphism in forensic analysis is not a "specific" use, as set forth in the Response to the Final Action, Appellants submit that this is improper on a number of different grounds. First, and most importantly, the Final Action seems to be confusing the requirements of a **specific** utility with a **unique** utility. The fact that other polymorphic markers have been identified in other genetic loci does not mean that Appellants' identification of a polymorphic marker in SEQ ID NO:1 is not specific. As clearly stated by the Federal Circuit in *Carl Zeiss Stiftung v. Renishaw PLC*, 20 USPQ2d 1101 (Fed. Cir. 1991):

> An invention need not be the best or only way to accomplish a certain result, and it need only be useful to some extent and in certain applications: "[T]he fact that an invention has only limited utility and is only operable in certain applications is not grounds for finding a lack of utility." *Envirotech Corp. v. Al George, Inc.*, 221 USPQ 473, 480 (Fed. Cir. 1984)

Just because other polymorphic sequences from the human genome have been described does not mean that the use of the presently described polymorphic markers for forensic analysis is not a specific utility. The requirement for a **specific** utility, which is the proper standard for utility under 35 U.S.C. § 101, should not be confused with the requirement for a **unique** utility, which is clearly an improper standard. If every invention were required to have a unique utility, the Patent and Trademark Office would no longer be issuing patents on batteries, automobile tires, golf balls, golf clubs, and treatments for a variety of human diseases, just to name a few particular examples, because examples of each of these have already been described and patented. However, only the briefest perusal of any issue of the Official Gazette provides numerous examples of patents being granted on each of the above compositions every week. Furthermore, if a composition needed to be unique to be patented, the entire class and subclass system would be an effort in futility, as the class and subclass system serves solely to group such common inventions, which would not be required if each invention needed to have a unique utility. Thus, the present sequence clearly

meets the requirements of 35 U.S.C. § 101.

Second, Appellants submit that the asserted forensic utility is specific because it cannot be applied to just any nucleic acid. In fact, the basis for forensic analysis is the fact that such a polymorphic marker is **not** present in all other nucleic acids, but in fact specific and unique to only a certain subset of the population. As such, the presently described polymorphic marker clearly has a specific utility, and therefore the presently claimed invention must meet the requirements for utility under 35 U.S.C. § 101.

It is important to note that it has been clearly established that a statement of utility in a specification must be accepted absent reasons why one skilled in the art would have reason to doubt the objective truth of such statement. *In re Langer*, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA, 1974; "*Langer*"); *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA, 1971). As clearly set forth in *Langer*:

> As a matter of Patent Office practice, a specification which contains a disclosure of utility which corresponds in scope to the subject matter sought to be patented must be taken as sufficient to satisfy the utility requirement of § 101 for the entire claimed subject matter unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope.

Langer at 297, emphasis in original. As set forth in the MPEP, "Office personnel must provide evidence sufficient to show that the statement of asserted utility would be considered 'false' by a person of ordinary skill in the art" (MPEP, Eighth Edition at 2100-40, emphasis added). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Furthermore, as the presently described polymorphism is a part of the family of polymorphisms that have a well established utility, the Federal Circuit's holding in *In re Brana,* (34 USPQ2d 1436 (Fed. Cir. 1995), "*Brana*") is directly on point. In *Brana*, the Federal Circuit admonished the Patent and Trademark Office for confusing "the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption". *Brana* at 1442. The Federal Circuit went on to state:

> At issue in this case is an important question of the legal constraints on patent office examination practice and policy. The question is, with regard to pharmaceutical inventions, what must the applicant provide regarding the practical utility or usefulness of the invention

> for which patent protection is sought. This is not a new issue; it is one which we would have thought had been settled by case law years ago.

Brana at 1439, emphasis added. The choice of the phrase "utility or usefulness" in the foregoing quotation is highly pertinent. The Federal Circuit is evidently using "utility" to refer to rejections under 35 U.S.C. § 101, and is using "usefulness" to refer to rejections under 35 U.S.C. § 112, first paragraph. This is made evident in the continuing text in *Brana*, which explains the correlation between 35 U.S.C. §§ 101 and 112, first paragraph. The Federal Circuit concluded:

> FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer.

Brana at 1442-1443, citations omitted, emphasis added. As set forth above, the present polymorphisms are useful in forensic analysis exactly as they are described in the specification as originally filed, without the need for any further research. Even if the use of these polymorphic markers provided additional information on the percentage of particular subpopulations that contain this polymorphic marker, this would not mean that "additional research" is needed in order for this marker as it is presently described in the instant specification to be of use to forensic science. As stated above, using the polymorphic marker as described in the specification as originally field will definitely distinguish members of a population from one another. However, even if, *arguendo*, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in *Brana*, which clearly states, as highlighted in the quote above, that "pharmaceutical inventions, necessarily includes the expectation of further research and development" (*Brana* at 1442-1443, emphasis added). In assessing the question of whether undue experimentation would be required in order to practice the claimed invention, the key term is "undue", not "experimentation". *In re Angstadt and Griffin*, 190 USPQ 214 (CCPA 1976). The need for some experimentation does not render the claimed invention

unpatentable. Indeed, a considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. *In re Angstadt and Griffin, supra*; *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991). As a matter of law, it is well settled that a patent need not disclose what is well known in the art. *In re Wands*, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Although Appellants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), Appellants pointed out in both the Response to the First Action and the Response to the Final Action that a sequence sharing over 99% percent identity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by third party scientists *wholly unaffiliated with Appellants* as "Homo sapiens gene for seven transmembrane helix receptor" (GenBank accession number AB065623; alignment provided in **Exhibit A**). The Final Action stated that "there is no sufficient and credible information that indicates the published sequence is a functional GPCR" (the Final Action at page 3). Appellants pointed out in the Response to the Final Action that an additional sequence sharing over 99% percent identity at the amino acid level over the entire length of the described sequence is present in the leading scientific repository for biological sequence data (GenBank), and has been annotated by different third party scientists *wholly unaffiliated with Appellants* as a "G-protein coupled receptor" (GenBank accession number BD144530; alignment provided in **Exhibit B**). The legal test for utility simply involves an assessment of whether those skilled in the art would find any of the utilities described for the invention to be credible or believable. Given these two GenBank annotations, there can be no question that those skilled in the art would clearly believe that Appellants' sequence is a G-protein coupled receptor. Thus, the present sequence clearly meets the requirements of 35 U.S.C. § 101.

The First Action denied that the extensive homology between Appellants' sequence and those sequences presented above confers a patentable utility to Appellants sequence, by questioning prediction of protein function based upon protein homology. In support of this allegation, the First Action cited Bork

and Koonin (1998, Nature Genetics *18*:313-318; "Bork and Koonin"), Ji *et al.* (1998, J. Biol. Chem. *273*:17299-17302; "Ji") and Yan *et al.* (2000, Science *290*:523-527; "Yan"). While these arguments were not set forth in either the Final Action or the Advisory Action, Appellants will again set forth the shortcomings of these articles, and point out the failure of these articles to support the alleged lack of utility of the presently claimed sequence.

First, with regard to the Bork and Koonin article, Bork and Koonin themselves conclude "(i)n summary, the currently available methods for sequence analysis are sophisticated, and while further improvements will certainly ensue, they are already capable of extracting subtle but functionally relevant signals from protein sequences (Bork and Koonin, page 317). Thus, the Bork and Koonin article is hardly indicative of a high level of uncertainty in assigning function based on sequence, and thus does not support the alleged lack of utility.

With regard to Ji, an exact quote from Ji completely undermines the question of asserted utility based upon protein homology: "a substantial degree of amino acid homology is found between members of a particular subfamily, but comparisons between subfamilies show significantly less or no similarity" (Ji at 17299, first paragraph, emphasis added). This quote suggests that homology with members of a G-protein coupled receptor is indicative that the particular sequence is in fact a member of that subfamily - the fact that there is little or no homology between subfamilies is completely irrelevant. Thus, Ji does not support the alleged lack of utility.

Furthermore, regarding Yan, this paper cites only one example, two isoforms of the anhidrotic ectodermal dysplasia (EDA) gene, where a two amino acid change conforms one isoform (EDA-A1) into the second isoform (EDA-A2). However, while it is true that this amino acid change results in binding to different receptors, it is important to note that the different receptors bound by the two isoforms are in fact related (Yan at page 523). Furthermore, the EDA-A2 receptor was correctly identified as a member of the tumor necrosis factor receptor superfamily based solely on sequence similarity (Yan at page 523). Thus, Yan does not suggest a high level of uncertainty in assigning function based on sequence, and thus also does not support the alleged lack of utility.

Rather, with regard to the utility of the presently claimed sequence, as 60% of the pharmaceutical

products currently being market by the entire industry target G-protein coupled receptors (Gurrath, 2001, Curr. Med. Chem. *8*:1605-1648; abstract presented in **Exhibit C**), a preponderance of the evidence clearly weighs in favor of Appellants' assertion that the skilled artisan would readily recognize that the presently described sequences have a specific (the claimed GPCR proteins are encoded by a specific locus on the human genome, see below), credible, and well-established utility, for example in tracking gene expression, as described in the specification as originally filed, at least at page 10, lines 13-16. In particular, the specification describes how the described sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934 (**Exhibit D**), 5,556,752 (**Exhibit E**), 5,744,305 (**Exhibit F**), 5,837,832 (**Exhibit G**), 6,156,501 (**Exhibit H**) and 6,261,776 (**Exhibit I**). Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies that have, at one time or another, concentrated on the use of gene sequences or fragments, in gene chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, one such company (Rosetta Inpharmatics) was viewed to have such "real world" value that it was acquired by large a pharmaceutical company (Merck) for significant sums of money (net equity value of the transaction was $620 million). The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section VIII(B), below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly,

compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action questioned this utility, stating "(s)ince the disclosure does not reveal any activity/functions of the nucleotide sequence or the protein encoded by the nucleotide sequence, one skilled in the art would not know how to use the claimed invention" (the Final Action at page 5). However, this argument is thwarted by the fact that skilled artisans already have used and continue to use sequences such as Appellants in gene chip applications. Appellants respectfully point out that this is exactly how most gene chip applications are carried out. Expression profiling does **not** require a knowledge of the function of the particular nucleic acid on the chip - rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Therefore, this argument also fails to support the alleged lack of utility of the presently claimed compositions.

Clearly, persons of skill in the art, as well as venture capitalists and investors, readily recognize the utility, both scientific and commercial, of genomic data in general, and specifically human genomic data. Billions of dollars have been invested in the human genome project, resulting in useful genomic data (see, *e.g.*, Venter *et al.*, 2001, Science *291*:1304; **Exhibit J**). The results have been a stunning success as the utility of human genomic data has been widely recognized as a great gift to humanity (see, *e.g.*, Jasny and Kennedy, 2001, Science *291*:1153; **Exhibit K**). Clearly, the usefulness of human genomic data, such as the presently claimed nucleic acid molecules, is substantial and credible (worthy of billions of dollars and the creation of numerous companies focused on such information) and well-established (the utility of human genomic information has been clearly understood for many years).

As yet a further example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 4, lines 24-26, the present nucleotide sequence has a specific utility in mapping the sequences to a specific region of a human chromosome. This is evidenced by the fact that SEQ ID NO:8 can be used to map the presently claimed sequence to chromosome 1 (present within the chromosome 1 clone, Genbank Accession Number AC091612; alignment and the first page from the Genbank report are presented in **Exhibit L**). Clearly, the present polynucleotide provides exquisite

specificity in localizing the specific region of human chromosome 1 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. For further evidence in support of the Appellants' position, the Board is requested to review, for example, section 3 of Venter *et al.* (*supra at* pp. 1317-1321, including Fig. 11 at pp.1324-1325; **Exhibit J**), which demonstrates the significance of expressed sequence information in the structural analysis of genomic data. The presently claimed polynucleotide sequence defines a biologically validated sequence that provides a unique and specific resource for mapping the genome essentially as described in the Venter *et al.* article Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Appellants respectfully remind the Board that only a minor percentage of the genome (2-4%) actually encodes exons, which in-turn encode amino acid sequences. The presently claimed polynucleotide sequence provides biologically validated empirical data (*e.g.*, showing which sequences are transcribed and polyadenylated) that *specifically* define that portion of the corresponding genomic locus that actually encodes exon sequence. Appellants respectfully submit that the practical scientific value of expressed and polyadenylated mRNA sequences is readily apparent to those skilled in the relevant biological and biochemical arts. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Regarding the utility requirements under 35 U.S.C. § 101, the Federal Circuit has clearly stated "(t)he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip Inc. v. Orange Bang Inc.*, 185 F.3d 1364, 51 USPQ2d 1700 (Fed. Cir. 1999) (citing *Brenner v. Manson*, 383 U.S. 519, 534 (1966)). Additionally, the Federal Circuit has stated that "(t)o violate § 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 USPQ2d 1401 (Fed. Cir. 1992), emphasis added. *Cross v. Iizuka* (753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985); "*Cross*")

states "any utility of the claimed compounds is sufficient to satisfy 35 U.S.C. § 101". *Cross* at 748, emphasis added. Indeed, the Federal Circuit recently emphatically confirmed that "anything under the sun that is made by man" is patentable *(State Street Bank & Trust Co. v. Signature Financial Group Inc.*, 149 F.3d 1368, 47 USPQ2d 1596, 1600 (Fed. Cir. 1998), citing the U.S. Supreme Court's decision in *Diamond vs. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (U.S., 1980)). Thus, based on the relevant case law, the present claims clearly meet the requirements of 35 U.S.C. § 101.

The Final Action also questioned the applicability of this case law, stating that "the Response cites a device case law" and "(t)hus, applicants' argument citing a case law regarding a device is irrelevant to the instant case" (the Final Action at page 3). Section 101 of the Patent Act of 1952, 35 U.S.C. § 101, provides that "[w]hoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof," may obtain a patent on the invention or discovery. Appellants point out that 35 U.S.C. § 101 covers devices (machines) as well as compositions, and makes no distinction between the two with regard to meeting the burden of complying with 35 U.S.C. § 101. Furthermore, the case law in question (*Juicy Whip Inc. v. Orange Bang Inc.*, 51 USPQ2d 1700 (Fed. Cir. 1999)) cites *Brenner v. Manson*, 383 U.S. 519, 534 (1966), which the Examiner obviously believes is not "irrelevant to the instant case", since the Examiner himself cites this exact case two times in the Final Action (see the Final Action at pages 3 and 5). Additionally, *Cross* and *Diamond vs. Chakrabarty, supra*, do not concern devices, but rather compositions. Thus, this argument completely fails to support the alleged lack of utility of the presently claimed compositions.

Finally, While Appellants are well aware of the new Utility Guidelines set forth by the USPTO, Appellants respectfully point out that the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Appellants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous

patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Board is invited to review U.S. Patent Nos. 5,817,479 (**Exhibit M**), 5,654,173 (**Exhibit N**), and 5,552,281 (**Exhibit O**; each of which claims short polynucleotides), and recently issued U.S. Patent No. 6,340,583 (**Exhibit P**; which includes no working examples), none of which contain examples of the "real-world" utilities that the Examiner seems to be requiring. Additionally, the Office has recently issued U.S. Patent 6,043,052 (**Exhibit Q**), which concerns an "orphan" G-Protein coupled receptor identified based only on homology to the orphan receptor GPR25, similar to the situation with Appellants' currently claimed sequence. Importantly, this issued patent also contains no examples of the "real world" utilities seemingly required in the present case. As issued U.S. Patents are presumed to meet all of the requirements for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section VIII(B), below), Appellants submit that the present polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Appellants understand that each application is examined on its own merits, Appellants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. Thus, holding Appellants to a different standard of utility would be arbitrary and capricious, and, like other clear violations of due process, cannot stand.

For each of the foregoing reasons, Appellants submit that the rejection of claims 1-3 under 35 U.S.C. § 101 must be overruled.

B. Are Claims 1-3 Unusable Due to a Lack of Patentable Utility?

The Final Action next rejects claims 1-3 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by either a clear asserted utility or a well-established utility.

The arguments detailed above in Section VIII(A) concerning the utility of the presently claimed sequences are incorporated herein by reference. As the Federal Circuit and its predecessor have

determined that the utility requirement of Section 101 and the how to use requirement of Section 112, first paragraph, have the same basis, specifically the disclosure of a credible utility (*In re Brana, supra*; *In re Jolles*, 628 F.2d 1322, 1326 n.11, 206 USPQ 885, 889 n.11 (CCPA 1980); *In re Fouche*, 439 F.2d 1237, 1243, 169 USPQ 429, 434 (CCPA 1971)), Appellants submit that as claims 1-3 have been shown to have "a specific, substantial, and credible utility", as detailed in Section VIII(A) above, the present rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, cannot stand.

Appellants therefore submit that the rejection of claims 1-3 under 35 U.S.C. § 112, first paragraph, must be overruled.

IX. APPENDIX

The claims involved in this appeal are as follows:

1. (Amended) An isolated expression vector comprising the nucleotide sequence of SEQ ID NO:8.

2. (Amended) An isolated expression vector comprising a nucleic acid sequence encoding the amino acid sequence of SEQ ID NO:9.

3. A host cell comprising the recombinant expression vector of claim 1 or 2.

X. CONCLUSION

Appellants respectfully submit that, in light of the foregoing arguments, the Final Action's conclusion that claims 1-3 lack a patentable utility and are unusable by the skilled artisan due to a lack of patentable utility is unwarranted. It is therefore requested that the Board overturn the Final Action's rejections.

Respectfully submitted,

June 11, 2003
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